was described by King (1972). Gibson *et al* (1974) described a patient with hypertrophic pulmonary osteoarthropathy localized to his feet. This man had an aortic graft inserted two years prior to onset of his symptoms and suffered from recurrent retroperitoneal sepsis.

Mr J B did not have hypertrophic pulmonary osteoarthropathy. How frequently clubbing is localized to the feet is not known. It may often not be looked for and it is sometimes difficult to be sure whether it is present or not.

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Wegener's Granulomatosis Presenting as Rheumatoid Arthritis (Two Cases)

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Wegener's granulomatosis is a rare disease of the upper and lower respiratory tract, usually accompanied by severe systemic complications. In 71 cases reported in the recent literature (Berman *et al.* 1963, Capizzi & Bertino 1971, Carrington & Liebow 1966, Cassan *et al.* 1970, Churg & Strauss 1951, Fauci & Wolff 1973, Fred *et al.* 1964, Godman & Churg 1954, Hollander & Manning 1967, Israel & Patchefsky 1971, McIlvanie 1966) disease of the upper or lower respiratory tract was the presenting feature in all but two: one (Capizzi & Bertino 1971) started as vasculitic skin lesions, the other (Israel & Patchefsky 1971) as fever and arthralgia. No cases are mentioned with prolonged prodromal symptoms. We report 2 cases which presented as typical rheumatoid arthritis a year or more before the onset of the classic respiratory signs and symptoms which enabled the true diagnosis to be made.

Case Histories

Case 1 Mrs M B, aged 45

Presented at the rheumatology clinic in the University Hospital of Wales in October 1974 giving a six-month history of generalized joint pains and stiffness. On examination there was a symmetrical polyarthritis of the metacarpophalangeal and proximal interphalangeal joints of the hands and feet, wrists, elbows and knees. A diagnosis of definite rheumatoid arthritis was made, as five of the ARA criteria were fulfilled, and the exclusions ruled out. She was treated with aspirin and hydroxychloroquine. At that time her ESR was 63 mm in 1 hour (Westergren), hæmoglobin 9.6 g/100 ml, DAT 1:16, ANF negative and chest X-ray normal.

Three weeks later she developed vasculitic lesions on the nail beds of her fingers and toes and the arthritis was worse. She was admitted to hospital, where she was treated with cyclophosphamide 50 mg twice daily in addition to standard analgesics. She made a good recovery and was discharged and was still in remission three months later when the cyclophosphamide was stopped due to a low white cell count. The arthritic symptoms returned four weeks later, and the gradual deterioration of her clinical condition started from this time.

In April 1975 she first complained of mastitis, sinusitis and nasal stuffiness. These symptoms grew steadily worse, and examination revealed nasal mucosal atrophy and crusting, with a fluid level in the left maxillary sinus. She also complained of some deafness in the left ear and of generalized left-sided facial pain. Over the next few weeks the latter remained the most prominent symptom, and it was extremely difficult to localize.

Local treatment for the nasal symptoms was started, then, as the lesions became more prolific, the possibility of Wegener's granulomatosis was raised. A chest X-ray at that time showed fluffy infiltrates in keeping with this diagnosis (Fig 1A).

On admission (June 1975): She was clearly very ill. There were widespread infected necrotic lesions on the skin, severe facial pain, dyspnœa, dysphagia and hoarseness, bloody diarrhœa and vaginal bleeding. Her hæmoglobin was 7.2 g/100 ml, ESR 104 mm in 1 hour, eosinophils 20% of 5000 white cells, but her urea and electrolytes were normal. More detailed examination showed that there were granulomatous lesions in the left tympanic membrane, vocal cords and vulva, but none was seen on colonoscopy to account for the diarrhœa and rectal bleeding. After initial treatment with four units of blood and antibiotics, she was restarted on oral cyclophosphamide 50 mg twice daily. Clinically her condition fluctuated for the next three weeks, complicated by bouts of melæna, dehydration, and further infections, but at the end of that time it was clear that she was improving slowly. The eosinophil count fell, and serial chest X-rays showed a steady clearing of the infiltrates (Fig 1B).

The cyclophosphamide dose was reduced to 50 mg daily due to a fall in the white cell count,

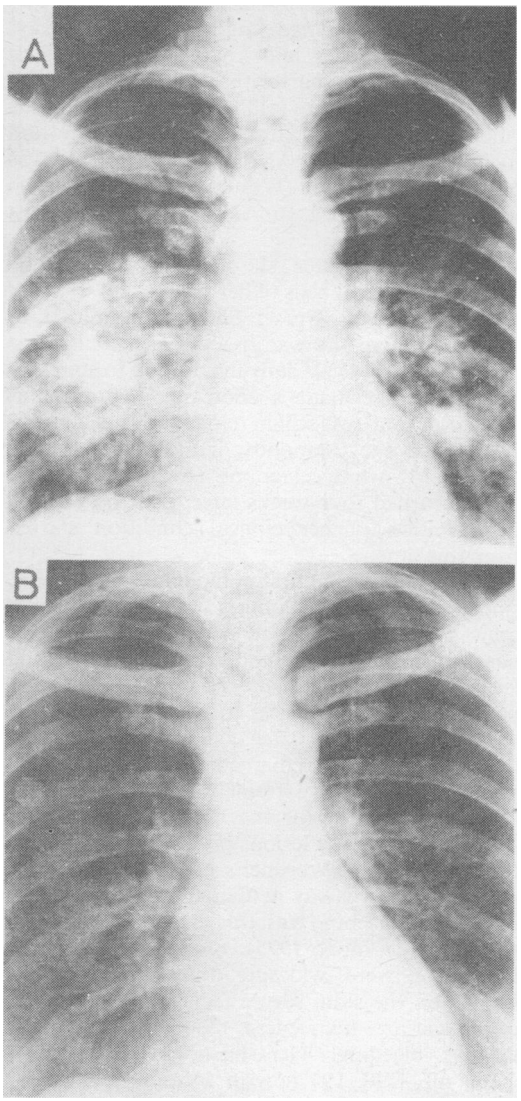

Fig 1 **Case 1** *Chest X-rays.* A, *May 1975, showing widespread infiltration.* B, *September 1975, after three months' treatment*

but was eventually stabilized at 75 mg daily, the dose she continues on to the present day.

Biopsies of the nasal mucosa and one of the skin lesions showed necrotic granulomata, with multinucleated giant cells, but minimal true vasculitis. This was in keeping with the diagnosis, which was made definitively on the combined clinical, radiological and histological findings. The skin biopsy was stained with fluorescent stains for immunoglobulins and complement, but only some streaky deposits of IgG were seen and no evidence of circulating immune complexes could be detected.

She was discharged in the middle of July 1975, and continued to improve slowly. The hæmoglobin stabilized at 12 g/100 ml and the ESR around 30 mm in 1 hour. The only residual symptoms have been persistent fluid in the middle ear cavities, which have required regular drainage; some deafness, and a slight change in the contour of her nose due to cartilage erosion. She has also had an attack of herpes zoster.

Case 2

Mrs P F, aged 75

Presented to the rheumatology department of Guy's Hospital in May 1970, with a six-month history of symmetrical inflammatory polyarthritis involving the feet, ankles, knees, shoulders, elbows, wrists, metacarpophalangeal and proximal interphalangeal joints. This was associated with subcutaneous nodules, vasculitic nailfold lesions, and a sensory neuropathy involving both feet. Her ESR was 107 mm in 1 hour (Westergren). She was weakly seropositive (DAT 1:32). X-rays of the hands revealed periarticular osteoporosis. The diagnosis of classical rheumatoid arthritis was made; because of the vasculitis she was treated with gold in addition to salicylates, with resolution of her arthritis and reversion of the latex rheumatoid factor to negative.

In October 1970 she had the first of a number of attacks of otitis media, and in August 1971 she developed hæmoptysis, with right-sided pleurisy accompanying a pleural effusion occurring in December of that year. Aspiration of pleural fluid and a pleural biopsy were performed, but did not enable a diagnosis to be made.

In March 1972 she had a recurrence of arthritis, which did not respond to a further course of gold. In May she developed her first episode of right-sided episcleritis, and also sinusitis. She was admitted to hospital in July 1972 with a symmetrical polyarthritis, scleral thinning and nasal obstruction. At the back of the nose, hyperæmic granular tissue covered with scabs was noted and a biopsy taken.

The biopsy material from the nose showed a necrotizing granuloma consistent with Wegener's granulomatosis. Her creatinine clearance was normal, a 24-hour urinary protein revealed no proteinuria and there was no urinary deposit. Her illness fitted the description of the limited form of Wegener's granulomatosis (Carrington & Liebow 1966) and in August 1972 she was started on prednisone 60 mg daily; azathioprine 250 mg and cyclophosphamide 100 mg daily were started in September and December respectively. The prednisone was tapered to a maintenance dose of 10 mg daily, and in February 1973 her azathioprine and cyclophosphamide were reduced to 100 mg and 50 mg respectively. She remained well

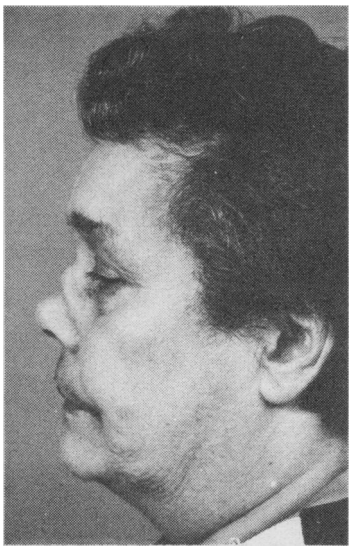

Fig 2 **Case 2** *photograph of lateral face of patient P F demonstrating typical 'saddle nose' deformity*

on this regime which was continued until April 1975 when the cytotoxic therapy was discontinued because of a fall in her platelet count to 90 000/mm³. She was continued on prednisone 6 mg daily, but her Wegener's granulomatosis flared up again in August with pleurisy, pericarditis, episcleritis and increased destruction of the nasal cartilage (Fig 2). Her ESR rose to 130 mm in 1 hour but renal function was again normal. Her prednisone was increased to 40 mg and she was again put on azathioprine with clinical improvement and fall of her ESR to normal levels. Attempts were made in December 1975 to reduce the daily dosage of prednisone, but when this fell to 12.5 mg the destruction of nasal cartilage accelerated and her ESR rose to 96 mm in 1 hour; her prednisone dosage was again, therefore, increased to 30 mg daily and she was started on cyclophosphamide 150 mg daily with good response, allowing the steroids to be tapered.

Discussion

As far as we know, the presentation of Wegener's granulomatosis by a prolonged inflammatory polyarthritis has not previously been reported, although a single patient in the series of 12 published by Israel & Patchefsky (1971) presented with fever and arthralgia for several weeks prior to the appearance of the respiratory tract disease. In virtually every other case the respiratory tract was involved at a very early stage, and was usually directly related to the presenting symptoms. Two points raised by these 2 cases merit discussion: (1) the concept of limited Wegener's granulomatosis, and (2) in view of the fact that the prodromal phase mimicked rheumatoid arthritis so closely, whether it is possible that a connexion exists between the two conditions.

It is possible that our patients did, in fact, have Wegener's granulomatosis superimposed on previous rheumatoid arthritis and there are several reports of this association (Bywaters & Scott 1965, Sturrock & Ratnesar 1974). It must be uncommon, however, for seronegative (or weakly seropositive) patients to present with widespread vasculitis, or for articular erosions to be absent up to five years after the onset of rheumatoid arthritis.

Traditionally, the diagnosis of Wegener's granulomatosis has required the presence of renal involvement (Godman & Churg 1954). Since then a limited form of the disease has been described, first by Carrington & Liebow (1966) who published a series of 16 cases, and then by Cassan *et al.* (1970) with 4 cases. None of their patients had overt renal disease. However, 6 of Carrington & Liebow's patients died of their disease, and at autopsy renal lesions were found in 5. Two out of 4 of Cassan's patients also died within three months of diagnosis. This suggests that the diagnosis of limited Wegener's granulomatosis cannot be made on clinical grounds alone, but requires a renal biopsy. Many clinicians are loath to do this in the absence of clinical renal disease or any clear indication that it would be of value in prognosis and we would argue that the term 'limited Wegener's granulomatosis' is, on present evidence, of limited value.

Both cases presented were limited by the present definition, but had widespread systemic features. Case 1 was at one stage extremely ill with widespread necrotic granulomata and fulminating disease, but renal disease was, at the most, transitory. Possibly treatment was initiated before the kidney had time to become seriously affected, but clearly there was generalized systemic involvement.

The original reason for defining a limited subgroup of this disease was largely because it was thought that the limited disease carried a better prognosis than the generalized form (Carrington & Liebow 1966). Now, however, with the use of cyclophosphamide and other cytotoxic drugs, the prognosis is excellent in all forms, and there is little reason to isolate a small group on these grounds. Reza *et al.* (1975) carried out renal biopsies on all 10 of his patients and found one patient without renal involvement, but the treatment was the same as in those with renal disease. Similarly, Fauci & Wolff (1973) treated their 18 patients in the same way whether there was kidney disease or not; 2 of their patients had abnormal renal biopsies despite normal function, with no urinary deposits.

Four of the cases described by Israel & Patchefsky were picked up on routine chest X-ray, and they were otherwise well and symptom free. This is in marked contrast to the general pattern of the disease where, at the very least, fever, malaise and weight loss would be expected. These patients had limited disease in the clinical sense, but even then one of the 4 later developed systemic symptoms, and the pulmonary lesions were progressive in 2 others. The response to azathioprine was excellent, after steroids had had no effect.

We would suggest that the concept of a limited form of the disease is unnecessary, and often misleading, as it may erroneously give the impression that a patient's prognosis is not bad enough to warrant cytotoxic drugs, and steroids may be given instead.

The particular features of our cases raise the question whether there is any connexion with rheumatoid arthritis. There are several similarities, and the point was considered by Carrington & Liebow (1966).

Systems which are involved in both Wegener's granulomatosis and rheumatoid arthritis include the joints, the skin or muscle, the eye, the respiratory tract, the heart or pericardium and the nervous system. In a series of 18 patients described by Fauci & Wolff (1973), 10 had arthralgia and 4 had arthritis. One patient had subcutaneous nodules, biopsy of which revealed granulomata without vasculitis; subcutaneous nodules were also present in 2 of the 16 patients with limited Wegener's granulomatosis described by Carrington & Liebow (1966). Rheumatoid factor was positive in 10 of Fauci & Wolff's patients (range 1:32 to 1:1024; mean 1:128). Biopsy of an inflamed ankle joint in a patient with Wegener's granulomatosis revealed chronic nonspecific inflammatory changes (Kinney *et al.* 1961), and Berman *et al.* (1963) described a synovial biopsy indicating acute synovitis with fibrinoid necrosis and granuloma formation.

On the other hand, in the majority of cases (Walton 1958) the pathology is diagnostic, although clinical similarities to other diffuse connective tissue diseases can be found in certain circumstances. For example, when pulmonary infiltrates and eosinophilia are predominant, there is a resemblance to polyarteritis nodosa.

There is no obvious explanation for the unusual presentation of these two cases, and it is rational to conclude that prolonged inflammatory polyarthritis is a further way in which this disease can present.

An argument must be made for adding Wegener's granulomatosis to the already extensive list of exclusions in the ARA criteria for diagnosing rheumatoid arthritis.

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The following case was also presented:

Acro-osteolysis Due to Vinyl Chloride

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